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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/991,150	11/16/2001	Avi J. Ashkenazi	P2730P1C48	4272
35489	7590	03/03/2004	EXAMINER	
HELLER EHRMAN WHITE & MCAULIFFE LLP			KEMMERER, ELIZABETH	
275 MIDDLEFIELD ROAD			ART UNIT	
MENLO PARK, CO 94025-3506			PAPER NUMBER	

1646

DATE MAILED: 03/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/991,150	Applicant(s) ASHKENAZI ET AL.	
	Examiner Elizabeth C. Kemmerer, Ph.D.	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 January 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 124-126, 129-131 and 135-138 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 124-126, 129-131 and 135-138 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The amendment received 07 January 2004 has been entered in full. Claims 1-123, 127, 128 and 132-134 are canceled. Claims 124-126, 129-131 and 135-138 are under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The application is now in compliance with the sequence rules.

The objection to the specification for containing embedded hyperlinks and for missing pages as set forth at p. 2 of the previous Office Action (Paper No. 6, 07 October 2003) is withdrawn in view of the amendment received 07 January 2004.

The rejection of claims 119-138 under 35 U.S.C. § 112, first paragraph (regarding enablement), as set forth at pp. 7-10 of the previous Office Action (Paper No. 6, 07 October 2003) is withdrawn in part. Specifically, the issue regarding the biological deposit has been resolved by Applicant's response (amendment received 07 January 2004).

The rejection of claims 119-123 and 132-138 under 35 U.S.C. § 112, first paragraph (regarding adequate written description), as set forth at pp. 10-12 of the previous Office Action (Paper No. 6, 07 October 2003) is withdrawn in view of the canceled and amended claims (amendment received 07 January 2004).

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The rejection of claims 119-124, 127, 128 and 132-138 under 35 U.S.C. § 112, second paragraph, as set forth at pp. 12-13 of the previous Office Action (Paper No. 6, 07 October 2003) is withdrawn in view of the canceled and amended claims (amendment received 07 January 2004).

The rejection of claims 132-133 under 35 U.S.C. § 102(e) as set forth at pp. 13-14 of the previous Office Action (Paper No. 6, 07 October 2003) is withdrawn in view of the canceled and amended claims (amendment received 07 January 2004).

35 U.S.C. §§ 101 and 112, First Paragraph

Claims 124-126, 129-131 and 135-138 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

Claims 124-126, 129-131 and 135-138 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

The basis for these rejections can be found at pp. 3-10 of the previous Office Action (Paper No. 6, 07 October 2003).

Applicant's arguments (pp. 6-9, amendment received 07 January 2004) have been fully considered but are not found to be persuasive for the following reasons.

Applicant states that the gene amplification assay provides utility and enablement for the claimed invention, and was first disclosed in provisional application 60/092182 filed July 9, 1998. Applicant explains how ΔCt values are calculated, and urges that a ΔCt value of 1 means a two fold increase over normal. Applicant refers to the specification which shows 1.12-1.33 ΔCt units for PRO341 in the gene amplification assay, which translated to a 2.173-2.514 fold amplification in lung tumors. Applicant refers to the Goddard declaration filed under 37 CFR 1.132 with the response as an expert opinion that a two fold increase is significant. The declaration is also described as stating that the gene amplification results set forth in Table 9A of the specification would lead one skilled in the art to find it credible that PRO341 nucleic acid is a diagnostic marker for human lung cancer. Applicant refers to the Ashkenazi declaration filed under 37 CFR 1.132 with the response as explaining why a control for aneuploidy is not critical. This has been fully considered but is not found to be persuasive. The declarations referred to by Applicant were not found attached to the response, or independently in the file. Applicant is requested to send copies of these declarations to complete the record. However, the declarations can be found in related cases 09/990,711, for example and have been considered in the interest of compact prosecution as they relate to the instant case. The declarations provided by Applicant in the related cases have clarified the assay and controls. However, Table 9A of the specification shows that PRO341 tested slightly positive in only 3 out of 14 lung tumor samples. After careful thought, it is concluded that one skilled in the art cannot conclude that such a weak correlation

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would indicate that PRO341 is a diagnostic marker for lung cancer. The art recognizes that lung epithelium is at risk for cellular damage due to direct exposure to environmental pollutants and carcinogens, which result in aneuploidy before the epithelial cells turn cancerous. See Hittelman (2001, Ann. N. Y. Acad. Sci. 952:1-12), who teach that damaged, precancerous lung epithelium is often aneuploid. See especially p. 4, Figure 4. The gene amplification assay does not provide a comparison between the lung tumor samples and normal lung epithelium, and thus it is not clear that PRO341 is amplified in cancerous lung epithelium more than in damaged (non-cancerous) lung epithelium. One skilled in the art would not conclude that PRO341 is a diagnostic probe for lung cancer unless it is clear that PRO341 is amplified to a clearly greater extent in true lung tumor tissue relative to non-cancerous lung epithelium. Also, while it might be argued in hindsight that PRO341 would still be a marker at least for precancerous, or damaged, lung epithelium, such is not suggested by the specification as originally filed and is not well-established in the *prior* art. Furthermore, the information given in Table 9A was generated using PCR primers that measured amplification of the coding region of SEQ ID NO: 19. However, the claims are broadly drawn to variants of SEQ ID NO: 19, including fragments and degenerate variants which have substitutions relative to SEQ ID NO: 19. One skilled in the art would expect that such variant sequences would lose their specificity as probes for the target sequence. Therefore, even if Applicant were to establish that the gene amplification assay provides utility and

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enablement for the coding region of SEQ ID NO: 19, the utility and enablement would not convey to the claimed variants.

For all of these reasons, the rejection under 35 U.S.C. §§ 101 and 112, first paragraph (enablement) are maintained.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (571) 272-0874. The examiner can normally be reached on Monday through Thursday, 7:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne L. Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Elizabeth C. Kemmerer

ECK

ELIZABETH KEMMERER
PRIMARY EXAMINER